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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,869	02/13/2002	Paul D. Robbins	AP32573-AAA 072396.0237	9884
21003 7590 01/17/2007 BAKER & BOTTS L.L.P. 30 ROCKEFELLER PLAZA 44TH FLOOR NEW YORK, NY 10112-4498			EXAMINER LUNDGREN, JEFFREY S	
			ART UNIT	PAPER NUMBER
			1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

Application No.

10/075,869

Applicant(s)

ROBBINS ET AL.

Examiner

Jeff Lundgren

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 51-65 is/are pending in the application.
- 4a) Of the above claim(s) 54, 59, 60 and 62-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 51 is/are allowed.
- 6) ☒ Claim(s) 52, 53, 55-58 and 61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 6, 2006, has been entered.

### ***Election/Restrictions***

Applicant's election without traverse of Group III (claims 51-65), and the required species, in the reply filed on September 5, 2006, is acknowledged.

Claims 51-65 are pending in the application; claims 54, 59, 60 and 62-65 are withdrawn as being directed to non-elected species. Claims 51-53, 55-58 and 61 are the subject of the Office Action below.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52-65 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 52-65 are indefinite for reciting the less conventional transitional language "is" to define the peptide-cargo complex because one of ordinary skill in the art could not reasonably determine the metes and bounds of the claimed complex. Specifically, it is not clear whether or not the "peptide" sequence that is being claimed can have additional amino acid residues attached. This rejection also applies to the use of the term "is" to define the sequence of the cargo within the peptide-cargo complex. Correction is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 52, 53 and 55-57, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zhang *et al.*, U.S. Patent No. 6,884,324, issued on January 18, 2005, in view of Goldstein *et al.*, WO 95/31999, published on November 30, 1995.

Claim 52 is directed to a peptide-cargo complex, comprising a peptide and a cargo wherein the sequence of the peptide is RRQRR (SEQ ID NO:97).

Zhang teaches a versatile and modular peptide mediated intracellular delivery system which is disclosed to be particularly adapted to facilitate the delivery of therapeutic compounds which are large in size or complex in nature. The invention relates both to a modular peptide mediated intracellular delivery system and a method of delivering a compound into a cell using the system. In Table 5 (col. 15), Zhang teaches peptide/cargo complexes, wherein the cargo complex has an apoptotic cargo (SEQ ID NO:41), which is attached to targeting peptide. Zhang suggest various attachment schemes of the cargo and peptide (col. 16, lines 1-18), and suggest the application of delivering cargo via a *TAT* peptide (paragraph bridging cols. 1 and 2). As in claims 56 and 57, the peptide facilitates cellular internalization and nuclear translocation.

Although Zhang suggests the application of this strategy with *TAT* peptides, Zhang does not explicitly state that the peptide component have the claimed amino acid sequence RRQRR (SEQ ID NO:97).

Goldstein teaches that uptake of TAT by cells is very strong, and teaches a peptide sequence having the sequence RRQRR (see page 2, SEQ ID NO:15). As in claim 53, the cargo is a polypeptide. As in claim 55, the peptide is apoptotic.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed, because each of Zhang and Goldstein are directed to developing compositions that facilitate the uptake of fusion peptides, and both recognize the fact that *TAT* peptides are highly desirable for such a purpose. One of ordinary skill in the art would have been motivated to utilize the *TAT* recognition site as taught by Goldstein in place of the recognition sequence of SEQ ID NO:41 of Zhang for targeting cells related to HIV transfection for delivering an proapoptosis peptide. Accordingly, the invention as claimed was *prima facie* obvious at the time it was invented.

Claims 52, 53, 55-57 and 61, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zhang *et al.*, U.S. Patent No. 6,884,324, issued on January 18, 2005, in view of Goldstein *et al.*, WO 95/31999, published on November 30, 1995, and Avrameas *et al.*, PNAS 95:5601-5606 (1998).

Claim 52 is directed to a peptide-cargo complex, comprising a peptide and a cargo wherein the sequence of the peptide is RRQRR (SEQ ID NO:97).

Zhang teaches a versatile and modular peptide mediated intracellular delivery system which is disclosed to be particularly adapted to facilitate the delivery of therapeutic compounds which are large in size or complex in nature. The invention relates both to a modular peptide mediated intracellular delivery system and a method of delivering a compound into a cell using the system. In Table 5 (col. 15), Zhang teaches peptide/cargo complexes, wherein the cargo complex has an apoptotic cargo (SEQ ID NO:41), which is attached to targeting peptide. Zhang suggest various attachment schemes of the cargo and peptide (col. 16, lines 1-18), and suggest the application of delivering cargo via a *TAT* peptide (paragraph bridging cols. 1 and 2). As in claims 56 and 57, the peptide facilitates cellular internalization and nuclear translocation.

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Although Zhang suggests the application of this strategy with *TAT* peptides, Zhang does not explicitly state that the peptide component have the claimed amino acid sequence RRQRR (SEQ ID NO:97). Although Zhang suggests the use of linkers between the cargo and peptide, Zhang does not explicitly suggest the use of a biotin-avidin bridge, as in claim 61.

Goldstein teaches that uptake of TAT by cells is very strong, and teaches a peptide sequence having the sequence RRQRR (see page 2, SEQ ID NO:15). As in claim 53, the cargo is a polypeptide. As in claim 55, the peptide is apoptotic.

Avrameas teaches the use of biotin-avidin bridges for linking peptide sequences for translocational delivery through a cellular membrane (see paragraph bridging page 5603 and 5604), as in claim 61.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed, because each of Zhang and Goldstein are directed to developing compositions that facilitate the uptake of fusion peptides, and both recognize the fact that *TAT* peptides are highly desirable for such a purpose. One of ordinary skill in the art would have been motivated to utilize the *TAT* recognition site as taught by Goldstein in place of the recognition sequence of SEQ ID NO:41 of Zhang for targeting cells related to HIV transfection for delivering an proapoptosis peptide. One of ordinary skill in the art would further have been motivated to utilize the biotin-avidin bridge as taught by Avrameas with the peptide-cargo complexes as suggested by Zhang and Goldstein because of the successful intracellular delivery of fusion peptides. Accordingly, the invention as claimed was *prima facie* obvious at the time it was invented.

### ***Conclusions***

Claim 51 is allowable; claims 52-65 are rejected.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipso verbis*, clarification on the record may be helpful). Should

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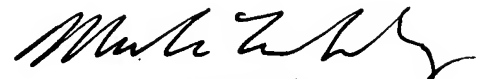
Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

  
MARK L. SHIBUYA  
PRIMARY EXAMINER